Clinical trial results:
A Randomized Double-Blind Phase 1b/2 Combined Staggered Multiple Dose Escalation Study of BOS161721 in Systemic Lupus Erythematosus (SLE) Patients on a Background of Limited Standard of Care

Summary

EudraCT number	2018-000305-23
Trial protocol	BG HU RO
Global end of trial date	26 November 2020

Results information

Result version number	v1 (current)
This version publication date	13 December 2021
First version publication date	13 December 2021

Trial information

Trial identification

Sponsor protocol code	BOS161721-02

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03371251
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boston Pharmaceuticals
Sponsor organisation address	55 Cambridge Parkway, Suite 400, Cambridge, MA , United States, 02142
Public contact	Etienne Dumont, Boston Pharmaceuticals, Inc., +1 (484) 986 8699,
Scientific contact	Etienne Dumont, Boston Pharmaceuticals, Inc., +1 (484) 986 8699,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	26 November 2020
Global end of trial reached?	Yes
Global end of trial date	26 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Multiple ascending doses (MAD) Phase 1b primary objective:
To assess safety, tolerability, and immunogenicity of repeat doses of BOS161721 (20, 60, and 120 mg) administered subcutaneously (SC) in adult subjects with moderate to severe systemic lupus erythematosus (SLE) on limited background standard of care treatment, in order to estimate the optimal dose.

Proof of Concept (POC) Phase 2 Primary Objective:

To demonstrate a superior effect of BOS161721 at the chosen dose compared with placebo for response on the SLE Responder Index 4 (SRI-4).

Protection of trial subjects:

Prior to the initiation of the study at each study center, the clinical study protocol, amendments, patient information sheet, Informed Consent Form (ICF), and all other relevant study documentation were submitted to and approved by the responsible Independent Ethics Committee (IEC)/Institutional Review Board (IRB).

The study was conducted in accordance with the principles set forth in the Declaration of Helsinki as amended in 2000, the Guidelines of the International Council for Harmonisation (ICH) on Good Clinical Practice (GCP) (CPMP/ICH/135/95), as well as the requirements of national drug and data protection laws, in particular the Health Insurance Portability and Accountability Act of 1996 (Public Law 104-191, 104th Congress), privacy regulations, and other applicable regulatory requirements.

Prior to undergoing any study specific procedure, each potential study subject provided signed acknowledgement of their freely given informed consent. If the subject was willing to participate in the study, the ICF was signed and personally dated by the subject, the physician taking the consent and, if applicable, the designated person who explained the nature of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 18
Country: Number of subjects enrolled	Bulgaria: 7
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	United States: 49
Country: Number of subjects enrolled	Georgia: 19
Country: Number of subjects enrolled	Argentina: 9

Country: Number of subjects enrolled	Colombia: 2
Country: Number of subjects enrolled	Mexico: 6
Country: Number of subjects enrolled	Peru: 29
Worldwide total number of subjects	143
EEA total number of subjects	29

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	131
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted in in the United States, Georgia, Bulgaria, Hungary, Poland, Argentina, Columbia, Mexico, Romania, Ukraine, Philippines and Peru. The first subject was screened on 10 January 2018 and last subject last visit occurred on 26, November 2020.

Pre-assignment

Screening details:

After successfully completing a screening phase, eligible subjects were randomized to a specified dose of BOS161721 or placebo. All assessments are screening phase were done as per the schedule of assessment table.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1b: Placebo

Arm description:

Subjects were randomized to receive subcutaneous (SC) dose of placebo. Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits at Days 210, 240, and 270.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was supplied for SC administration

Arm title	Phase 1b: Cohort 1: BOS161721 20 mg

Arm description:

Subjects were randomized to receive a 20 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Arm type	Experimental
Investigational medicinal product name	BOS161721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

BOS161721 was supplied for SC administration

Arm title	Phase 1b: Cohort 2: BOS161721 60 mg

Arm description:

Subjects were randomized to receive a 60 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Arm type	Experimental
Investigational medicinal product name	BOS161721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

BOS161721 was supplied for SC administration

Arm title	Phase 1b: Cohort 3: BOS161721 120 mg

Arm description:

Subjects were randomized to receive a 120 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Arm type	Experimental
Investigational medicinal product name	BOS161721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

BOS161721 was supplied for SC administration

Arm title	Phase 2: Placebo

Arm description:

Subjects were randomized to receive a SC dose of placebo (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Placebo was supplied for SC administration

Arm title	Phase 2: BOS161721 120 mg

Arm description:

Subjects were randomized to receive a 120 mg SC dose of BOS161721 (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Arm type	Experimental
Investigational medicinal product name	BOS161721
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

BOS161721 was supplied for SC administration

Number of subjects in period 1	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg
Started	7	5	9
Completed	5	5	8
Not completed	2	0	1
Consent withdrawn by subject	1	-	1
Phase 1b: Pregnancy, Phase 2: fear of COVID- 19	1	-	-
Decision by Sponsor	-	-	-
Adverse event	-	-	-

Number of subjects in period 1	Phase 1b: Cohort 3: BOS161721 120 mg	Phase 2: Placebo	Phase 2: BOS161721 120 mg
Started	9	37	76
Completed	9	30	71
Not completed	0	7	5
Consent withdrawn by subject	-	2	2
Phase 1b: Pregnancy, Phase 2: fear of COVID- 19	-	2	3
Decision by Sponsor	-	2	-
Adverse event	-	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Phase 1b: Placebo
Reporting group description:	
Subjects were randomized to receive subcutaneous (SC) dose of placebo. Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits at Days 210, 240, and 270.	
Reporting group title	Phase 1b: Cohort 1: BOS161721 20 mg
Reporting group description:	
Subjects were randomized to receive a 20 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 1b: Cohort 2: BOS161721 60 mg
Reporting group description:	
Subjects were randomized to receive a 60 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 1b: Cohort 3: BOS161721 120 mg
Reporting group description:	
Subjects were randomized to receive a 120 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 2: Placebo
Reporting group description:	
Subjects were randomized to receive a SC dose of placebo (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 2: BOS161721 120 mg
Reporting group description:	
Subjects were randomized to receive a 120 mg SC dose of BOS161721 (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	

Reporting group values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg
Number of subjects	7	5	9
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean	48.1	50.0	49.3
standard deviation	± 17.67	± 8.51	± 11.31

Gender categorical Units: Subjects			
Female	7	5	8
Male	0	0	1

Reporting group values	Phase 1b: Cohort 3: BOS161721 120 mg	Phase 2: Placebo	Phase 2: BOS161721 120 mg
Number of subjects	9	37	76
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	47.3	45.7	44.5
standard deviation	± 10.43	± 12.52	± 12.52
Gender categorical Units: Subjects			
Female	8	36	69
Male	1	1	7

Reporting group values	Total		
Number of subjects	143		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical Units: Subjects			
Female	133		
Male	10		

End points

End points reporting groups

Reporting group title	Phase 1b: Placebo
Reporting group description:	
Subjects were randomized to receive subcutaneous (SC) dose of placebo. Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits at Days 210, 240, and 270.	
Reporting group title	Phase 1b: Cohort 1: BOS161721 20 mg
Reporting group description:	
Subjects were randomized to receive a 20 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 1b: Cohort 2: BOS161721 60 mg
Reporting group description:	
Subjects were randomized to receive a 60 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 1b: Cohort 3: BOS161721 120 mg
Reporting group description:	
Subjects were randomized to receive a 120 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 2: Placebo
Reporting group description:	
Subjects were randomized to receive a SC dose of placebo (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	
Reporting group title	Phase 2: BOS161721 120 mg
Reporting group description:	
Subjects were randomized to receive a 120 mg SC dose of BOS161721 (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.	

Primary: Phase 1b: Number of Subjects With Adverse Events (AEs)

End point title	Phase 1b: Number of Subjects With Adverse Events (AEs)[1][2]
End point description:	
The safety, tolerability, and immunogenicity of repeat doses of BOS161721 (20, 60, and 120 mg) administered SC were assessed in adult subjects with moderate to severe SLE on limited background standard of care treatment, in order to estimate the optimal dose.	
End point type	Primary
End point timeframe:	
Up to Day 270	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical tests planned due to small sample size per cohort

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the primary endpoint for phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: Subjects				
number (not applicable)				
Any Treatment-Emergent Adverse Events (TEAE)	4	2	7	8
Related TEAE	1	0	1	0
Serious TEAE	1	0	2	0
Related Serious TEAE	0	0	0	0
CTCAE Grade 2 or Higher TEAE	4	2	6	7
Any Related CTCAE Grade 2 or Higher TEAE	1	0	0	0
Any CTCAE Grade 3 TEAE	1	1	2	0
Any Related CTCAE Grade 3 or Higher TEAE	0	0	0	0
Any CTCAE Grade 4 TEAE	0	0	0	0
TEAE Leading to Discontinuation of Study Treatment	0	0	0	0
Related TEAE Leading to Discont of Study Treatment	0	0	0	0
TEAE of Special Interest	0	0	0	0
Related TEAE of Special Interest	0	0	0	0
Dose-Limiting Toxicity	0	0	0	0
Related Dose-Limiting Toxicity	0	0	0	0
TEAE Resulting in Death	0	0	0	0
Related TEAE Resulting in Death	0	0	0	0
Injection Site Reaction	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Number of Subjects With an SLE Responder Index 4 (SRI-4) Response at Day 210

End point title	Phase 2: Number of Subjects With an SLE Responder Index 4 (SRI-4) Response at Day 210[3]

End point description:

The SRI-4 is a composite index of SLE disease improvement that consists of scores derived from the SLE Disease Activity Index 2000 (SLEDAI-2K), the British Isles Lupus Assessment Group (BILAG) 2004 Index and the Physician's Global Assessment (PGA). Response based on the SRI-4 is defined by: 1) ≥ 4-point reduction in the SLEDAI-2K total score; 2) no new severe disease activity (BILAG A organ score) or more than 1 new moderate organ score (BILAG B) compared with baseline; and 3) no deterioration from baseline in the PGA by ≥ 30 millimeters. The SLEDAI-2K total score falls between 0 and 105, with higher scores representing increased disease activity. The SRI-4 response in subjects with moderate to severe SLE is associated with broad improvements in clinical and subject-reported outcomes.

End point type	Primary

End point timeframe:

Day 210

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the primary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Subjects				
number (not applicable)				
SRI-4 Response	19	40		
≥ 4-Point Reduction from Baseline SLEDAI-2K score	19	40		
No New BILAG A or More than One BILAG B OrganScore	27	68		
No Deterioration from Baseline in PGA by >=30mm	27	68		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Statistical Analysis: SRI-4 Response	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8434
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.5
upper limit	18.5

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Statistical Analysis: >= 4-Point Reduction from Baseline in SLEDAI-2K Global Score	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8434
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	2
Confidence interval	
level	90 %
sides	2-sided
lower limit	-14.5
upper limit	18.5

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Statistical Analysis: No New BILAG A or More than One BILAG B Organ Score Compared with Baseline	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0141
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	17.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	4.5
upper limit	30.9

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Statistical Analysis: No Deterioration from Baseline in PGA by >=30mm	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0141
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	17.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	4.5
upper limit	30.9

Secondary: Phase 1b: Maximum Observed Concentration (Cmax)

End point title	Phase 1b: Maximum Observed Concentration (Cmax)[4]

End point description:

The PK of BOS161721 was characterized and the optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE. n signifies only the subjects with available data for each dose.

End point type	Secondary

End point timeframe:

Pre-dose: Days 0, 30, 60, 90, 120, 150, and 180. Post-dose: Days 0, 7, 15, 30, 180, 187, 195, 210, 240, and 270. Post-dose samples were collected at 4, 8, and 24 hours after study drug administration on Days 0, 30, and 180

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	9	9	
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Dose 1 (n=4, 8, 9)	1160 (± 42.0)	4610 (± 54.8)	5500 (± 52.3)	
Dose 2 (n=5, 8, 9)	1240 (± 23.9)	5670 (± 35.7)	7580 (± 45.1)	
Dose 7 (n=5, 8, 9)	2580 (± 19.1)	7820 (± 144)	20300 (± 37.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: First Time to Maximum Concentration (Tmax)

End point title	Phase 1b: First Time to Maximum Concentration (Tmax)[5]

End point description:

The PK of BOS161721 was characterized and the optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE. n signifies only the subjects with available data for each dose.

End point type	Secondary

End point timeframe:

Pre-dose: Days 0, 30, 60, 90, 120, 150, and 180. Post-dose: Days 0, 7, 15, 30, 180, 187, 195, 210, 240, and 270. Post-dose samples were collected at 4, 8, and 24 hours after study drug administration on Days 0, 30, and 180

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	9	9	
Units: Day				
median (full range (min-max))				
Dose 1 (n= 4, 8, 9)	7.01 (6.99 to 12.00)	7.00 (5.93 to 15.00)	8.04 (6.95 to 17.04)	
Dose 2 (n= 5, 8, 9)	1.04 (1.00 to 29.02)	1.00 (0.99 to 34.97)	1.00 (1.00 to 33.03)	
Dose 7 (n= 5, 8, 9)	6.18 (5.03 to 20.04)	3.55 (0.91 to 12.00)	8.96 (1.00 to 28.06)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: The Area Under the Plasma Concentration Versus Time Curve, From Time 0 to the Last Quantifiable Concentration (AUClast)

End point title	Phase 1b: The Area Under the Plasma Concentration Versus Time Curve, From Time 0 to the Last Quantifiable Concentration (AUClast)[6]

End point description:

The PK of BOS161721 was characterized and the optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE. n signifies only the subjects with available data for each dose.

End point type	Secondary

End point timeframe:

Pre-dose: Days 0, 30, 60, 90, 120, 150, and 180. Post-dose: Days 0, 7, 15, 30, 180, 187, 195, 210, 240, and 270. Post-dose samples were collected at 4, 8, and 24 hours after study drug administration on Days 0, 30, and 180

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	9	9	
Units: day*ng/mL				
geometric mean (geometric coefficient of variation)				
Dose 1 (n= 4, 8, 9)	25100 (± 40.4)	89400 (± 51.7)	124000 (± 40.5)	
Dose 2 (n= 5, 8, 9)	33600 (± 18.2)	147000 (± 29.7)	229000 (± 47.9)	
Dose 7 (n= 5, 8, 9)	155000 (± 17.9)	460000 (± 173)	1400000 (± 38.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Terminal Elimination Half-life (t1/2)

End point title	Phase 1b: Terminal Elimination Half-life (t1/2)[7]

End point description:

The PK of BOS161721 was characterized and the optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE. n signifies only the subjects with available data for each dose.
999.99 = Not calculated for 1 subject

End point type	Secondary

End point timeframe:

Pre-dose: Days 0, 30, 60, 90, 120, 150, and 180. Post-dose: Days 0, 7, 15, 30, 180, 187, 195, 210, 240, and 270. Post-dose samples were collected at 4, 8, and 24 hours after study drug administration on Days 0, 30, and 180

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	1	
Units: Day				
geometric mean (geometric coefficient of variation)	75.2 (± 19.9)	66.3 (± 35.4)	64.3 (± 999.99)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Apparent Plasma Clearance After Extravascular Administration (CL/F)

End point title	Phase 1b: Apparent Plasma Clearance After Extravascular Administration (CL/F)[8]

End point description:

The PK of BOS161721 was characterized and the optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE. n signifies only the subjects with available data for each dose.

End point type	Secondary

End point timeframe:

Pre-dose: Days 0, 30, 60, 90, 120, 150, and 180. Post-dose: Days 0, 7, 15, 30, 180, 187, 195, 210, 240, and 270. Post-dose samples were collected at 4, 8, and 24 hours after study drug administration

on Days 0, 30, and 180

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	8	9	
Units: Liter/day				
geometric mean (geometric coefficient of variation)	0.289 (± 18.3)	0.311 (± 179)	0.218 (± 38.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Apparent Volume of Distribution After Extravascular Administration (Vz/F)

End point title	Phase 1b: Apparent Volume of Distribution After Extravascular Administration (Vz/F)[9]

End point description:

The PK of BOS161721 was characterized and the optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE. n signifies only the subjects with available data for each dose.
999.99 = Not calculated for 1 subject

End point type	Secondary

End point timeframe:

Pre-dose: Days 0, 30, 60, 90, 120, 150, and 180. Post-dose: Days 0, 7, 15, 30, 180, 187, 195, 210, 240, and 270. Post-dose samples were collected at 4, 8, and 24 hours after study drug administration on Days 0, 30, and 180

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	5	5	1	
Units: Liter				
geometric mean (geometric coefficient of variation)	31.4 (± 33.2)	18.5 (± 39.6)	23.0 (± 999.99)	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean Change From Baseline in Phosphorylated Signal Transducer and Activator of Transcription 3 (pSTAT3)

End point title	Phase 1b: Mean Change From Baseline in Phosphorylated Signal Transducer and Activator of Transcription 3 (pSTAT3)[10]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and pharmacodynamic (PD) effects in subjects with moderate to severe SLE.
mean change in % pSTAT3+ Lymphocytes - Stimulated, Day 30: n = 6,5,8,9
mean change in % pSTAT3+ Lymphocytes - Stimulated, Day 44: n = 6,5,8,9
mean change in % pSTAT3+ Lymphocytes -Stimulated, Day 60: n = 6,5,8,9
mean change in % pSTAT3+ Lymphocytes - Stimulated, Day 90: n= 5,5,8,9
Here, n signifies only the subjects with available data for each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 0); Days 30, 44, 60, and 90 (pre-dose [trough] samples only)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: Percentage				
arithmetic mean (standard deviation)				
% pSTAT3+ Lymphocytes - Stimulated, Day 30	12.72 (± 25.172)	-41.80 (± 24.631)	-31.35 (± 20.281)	-25.73 (± 20.895)
% pSTAT3+ Lymphocytes - Stimulated, Day 44	18.45 (± 24.025)	-60.00 (± 19.672)	-32.99 (± 19.899)	-26.57 (± 20.856)
% pSTAT3+ Lymphocytes - Stimulated, Day 60	-1.48 (± 19.129)	-59.46 (± 20.310)	-32.68 (± 19.214)	-25.91 (± 20.850)
% pSTAT3+ Lymphocytes - Stimulated, Day 90	-15.94 (± 34.757)	-67.48 (± 15.630)	-33.03 (± 19.637)	-26.74 (± 20.962)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean Change From Baseline in Compliment 3 (C3) and Compliment (C4) Levels

End point title	Phase 1b: Mean Change From Baseline in Compliment 3 (C3) and Compliment (C4) Levels[11]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE.
n signifies only the subjects with available data for each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 0); Days 210

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: gram/Litre				
arithmetic mean (standard deviation)				
C3, Day 210 (n=5,5,8,9)	0.094 (± 0.2289)	-0.032 (± 0.0876)	0.050 (± 0.3424)	-0.078 (± 0.2879)
C4, Day 210 (n=5,5,8,9)	0.024 (± 0.0391)	-0.038 (± 0.0370)	-0.007 (± 0.0783)	-0.024 (± 0.0410)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean Change From Baseline in Leukocyte Immunophenotype

End point title	Phase 1b: Mean Change From Baseline in Leukocyte Immunophenotype[12]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE.

End point type	Secondary

End point timeframe:

Baseline (Day 0); Day 180

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: Change				
arithmetic mean (standard deviation)				
CD19+% of CD45+ Lymphocytes	-2.07 (± 3.201)	-5.34 (± 4.663)	-0.39 (± 4.201)	0.27 (± 3.481)
CD25+CD127-% of CD4+CD8-	-1.03 (± 1.388)	-0.22 (± 2.406)	-0.38 (± 1.495)	-1.08 (± 2.266)
CD4+CD8-% of CD3+	-1.01 (± 10.866)	-3.08 (± 5.272)	0.88 (± 7.434)	-5.04 (± 7.671)
CD56+% OF CD45+ Lymphocytes	-0.56 (± 2.093)	-5.76 (± 4.231)	-2.38 (± 2.461)	2.04 (± 7.984)

CD8+CD4-% of CD3+	-3.00 (± 7.792)	-1.38 (± 4.467)	-2.92 (± 5.010)	-0.24 (± 6.517)
CXCR5+% of CD25+CD127-	0.20 (± 4.676)	7.02 (± 3.371)	10.62 (± 11.963)	0.63 (± 5.915)
CXCR5+% of CD4+CD8-	0.81 (± 12.373)	15.18 (± 7.564)	13.14 (± 16.091)	-0.69 (± 7.208)
ICOS+% of CD25+CD127-	8.59 (± 10.618)	1.56 (± 3.840)	12.93 (± 11.905)	4.27 (± 17.059)
ICOS+% of CD4+CD8-	3.93 (± 6.906)	0.14 (± 5.227)	5.01 (± 5.053)	0.54 (± 15.534)
IgD+C27-% of CD19+	0.20 (± 7.127)	2.42 (± 5.882)	-1.07 (± 4.748)	-0.80 (± 6.031)
IgD+CD27+% of CD19+	1.29 (± 1.785)	-3.24 (± 6.080)	-1.24 (± 2.823)	1.00 (± 3.260)
IgD+CD27-CD38++CD24++% of CD19+	0.50 (± 1.262)	0.56 (± 1.688)	-0.42 (± 2.351)	0.16 (± 1.385)
IgD-CD27+% of CD19+	-0.21 (± 3.866)	-0.48 (± 3.891)	2.02 (± 3.751)	0.70 (± 3.740)
IgD-CD27+CD38++CD138+% of CD19+	0.03 (± 0.049)	0.04 (± 0.089)	0.08 (± 0.172)	-0.02 (± 0.130)
IgD-CD27+CD38++CD138-% of CD19+	-0.20 (± 0.432)	-0.20 (± 0.354)	0.59 (± 1.437)	-0.63 (± 1.081)
IgD-CD27-% of CD19+	-1.29 (± 2.963)	1.36 (± 2.373)	0.32 (± 2.059)	-0.83 (± 1.648)
PD-1+% of CD25+CD127-	0.31 (± 6.093)	3.30 (± 5.039)	7.41 (± 6.064)	-8.49 (± 13.258)
PD-1+% of CD4+CD8-	-0.07 (± 6.366)	4.14 (± 4.146)	6.39 (± 5.882)	-9.01 (± 13.036)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean Change From Baseline in Anti-double-stranded DNA (dsDNA) Autoantibodies at Each Visit

End point title	Phase 1b: Mean Change From Baseline in Anti-double-stranded DNA (dsDNA) Autoantibodies at Each Visit[13]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE.
n signifies only the subjects with available data for each time point.

End point type	Secondary

End point timeframe:

Baseline (Day 0); Days 30, 60, 90, 120, 150, 180, 210, 240, and 270

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: International units per millilitre				
arithmetic mean (standard deviation)				
Day 30 (n= 7,5,8,9)	-1.11 (± 3.504)	0.48 (± 0.410)	5.34 (± 9.053)	-11.51 (± 32.444)
Day 60 (n=7,5,8,9)	-1.81 (± 5.048)	0.40 (± 0.376)	8.06 (± 18.430)	-6.11 (± 15.612)
Day 90 (n=6,5,8,9)	0.15 (± 0.448)	0.00 (± 0.187)	19.31 (± 48.594)	-13.44 (± 35.152)
Day 120 (n=6,5,8,9)	-0.02 (± 0.270)	0.41 (± 0.598)	12.30 (± 35.583)	-15.58 (± 47.248)
Day 150 (n=5,5,8,9)	-0.03 (± 0.199)	0.62 (± 0.709)	17.39 (± 50.086)	-11.18 (± 38.152)
Day 180 (n=7,5,9,9)	-2.13 (± 5.905)	0.52 (± 0.584)	8.00 (± 21.169)	-17.13 (± 49.897)
Day 210 (n=5,5,8,9)	0.05 (± 0.359)	0.07 (± 0.540)	6.76 (± 20.173)	-17.96 (± 50.274)
Day 240 (n=5,5,8,9)	0.07 (± 0.428)	0.34 (± 1.117)	6.81 (± 21.903)	-18.35 (± 47.898)
Day 270 (n=7,5,8,9)	-1.94 (± 4.974)	0.37 (± 0.700)	7.99 (± 24.116)	-9.71 (± 27.833)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean change From Baseline in Anti-Sjögren syndrome A and B (SSA, SSB)

End point title	Phase 1b: Mean change From Baseline in Anti-Sjögren syndrome A and B (SSA, SSB)[14]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE.

End point type	Secondary

End point timeframe:

Baseline (Day 0); Day 180

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: U/mL				
arithmetic mean (standard deviation)				

La Antibody	0.04 (± 0.175)	0.11 (± 0.108)	1.02 (± 2.639)	0.47 (± 1.668)
Sjogrens SS-A52 Antibody	-0.04 (± 0.128)	0.05 (± 0.112)	0.19 (± 0.567)	-2.25 (± 4.861)
Sjogrens SS-A60 Antibody	0.00 (± 0.000)	0.00 (± 0.000)	-2.62 (± 7.867)	-4.36 (± 8.684)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean change From Baseline in Anti-Smith antibody (Sm)

End point title	Phase 1b: Mean change From Baseline in Anti-Smith antibody (Sm)[15]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE.

End point type	Secondary

End point timeframe:

Baseline (Day 0); Day 180

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: U/mL				
arithmetic mean (standard deviation)	-1.87 (± 4.827)	0.74 (± 0.391)	-3.21 (± 9.419)	3.61 (± 19.504)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean Change From Baseline in Antiphospholipid (APL) autoantibodies (Beta 2 glycoprotein, cardiolipin IgG)

End point title	Phase 1b: Mean Change From Baseline in Antiphospholipid (APL) autoantibodies (Beta 2 glycoprotein, cardiolipin IgG)[16]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE.

End point type	Secondary

End point timeframe:

Baseline (Day 0); Day 180

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: U/mL				
arithmetic mean (standard deviation)				
Anti-Cardiolipin IgG Antibody	-0.03 (± 0.412)	3.55 (± 5.559)	0.07 (± 0.585)	-0.42 (± 0.180)
Beta-2 Glycoprotein 1 IgG Antibody	-0.11 (± 0.358)	-7.48 (± 23.684)	-0.14 (± 0.882)	0.02 (± 0.787)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b: Mean Change From Baseline in Abrogation of IL-21 Gene Signature

End point title	Phase 1b: Mean Change From Baseline in Abrogation of IL-21 Gene Signature[17]

End point description:

The optimal dose of BOS161721 was selected based on safety, tolerability, PK and PD data in subjects with moderate to severe SLE.
99.999 = Data were not analyzed for this endpoint

End point type	Secondary

End point timeframe:

Baseline (Day 0); Days 15, 90, 180, and 270

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 1b only

End point values	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg	Phase 1b: Cohort 3: BOS161721 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	7	5	9	9
Units: Percentage				
arithmetic mean (standard deviation)	99.999 (± 99.999)	99.999 (± 99.999)	99.999 (± 99.999)	99.999 (± 99.999)

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With an SRI-4, SRI-5, and SRI-6 Response at Each Visit

End point title	Phase 2: Number of Subjects With an SRI-4, SRI-5, and SRI-6 Response at Each Visit[18]

End point description:

The SRI-4 is a composite index of SLE disease improvement that consists of scores derived from the SLE Disease Activity Index 2000 (SLEDAI-2K) and the British Isles Lupus Assessment Group (BILAG) 2004 Index. Response based on the SRI-4 is defined by: 1) ≥ 4-point reduction in the SLEDAI-2K global score; 2) no new severe disease activity (BILAG A organ score) or more than 1 new moderate organ score (BILAG B); and 3) no deterioration from baseline in the Physician's Global Assessment (PGA) by ≥ 30 millimeters. The SRI-4 response in subjects with moderate to severe SLE is associated with broad improvements in clinical and subject-reported outcomes. SRI-5 and SRI-6 are composite indices of SLE disease improvement that consist of scores derived from the SLEDAI-2K and the BILAG 2004 Index. The SRI-5 and SRI-6 are computed with a minimal five-point or six-point improvement in SLEDAI-2K being required, respectively.
n signifies only the subjects with available data for each time point.

End point type	Secondary

End point timeframe:

Days 30, 60, 90, 120, 150, 180, 210, 240, and 270

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Subjects				
number (not applicable)				
SRI-4, Day 30 (n=36, 73)	5	0		
SRI-4, Day 60 (n=35, 71)	11	15		
SRI-4, Day 90 (n= 35, 65)	15	24		
SRI-4, Day 120 (n=35, 66)	17	29		
SRI-4, Day 150 (n=35, 71)	19	35		
SRI-4, Day 180 (n=35, 72)	20	37		
SRI-4, Day 210 (n=37, 75)	19	40		
SRI-5, Day 30 (n= 36, 73)	2	0		
SRI-5, Day 60 (n=35, 71)	1	10		
SRI-5, Day 90 (n= 35, 65)	3	15		
SRI-5, Day 120 (n= 35, 66)	8	15		
SRI-5, Day 150 (n= 35, 71)	15	22		
SRI-5, Day 180 (n= 35, 72)	14	29		
SRI-5, Day 210 (n= 37, 75)	17	29		
SRI-6, Day 30 (n= 36, 73)	1	0		
SRI-6, Day 60 (n= 35, 71)	1	10		
SRI-6, Day 90 (n=35, 65)	3	15		
SRI-6, Day 120 (n= 35, 66)	8	14		
SRI-6, Day 150 (n= 35, 71)	15	22		
SRI-6, Day 180 (n= 35, 72)	14	28		
SRI-6, Day 210 (n= 37, 75)	17	29		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Number of Subjects With a Sustained Reduction From Baseline of Oral Corticosteroid (CS) (≤ 7.5 mg/Day and < Day 0 Dose) Between Day 150 and Day 210

End point title	Phase 2: Number of Subjects With a Sustained Reduction From Baseline of Oral Corticosteroid (CS) (≤ 7.5 mg/Day and < Day 0 Dose) Between Day 150 and Day 210[19]

End point description:

Effect of BOS161721 compared with placebo for response on clinical indicators of SLE activity was assessed in adult subjects with moderate to severe SLE on limited background standard of care treatment.
Here subjects analysed signifies only the number of subjects taking oral corticosteroids at baseline.

End point type	Secondary

End point timeframe:

Day 150 to Day 210

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	67		
Units: Subjects				
number (not applicable)	7	17		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7985
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	-2.6

Confidence interval	
level	90 %
sides	2-sided
lower limit	-19.8
upper limit	14.5

Secondary: Phase 2: Number of Subjects With New or Recurrent BILAG Flares (≥ 1 Qualifying BILAG A or > 1 Qualifying BILAG B) Through Day 210

End point title	Phase 2: Number of Subjects With New or Recurrent BILAG Flares (≥ 1 Qualifying BILAG A or > 1 Qualifying BILAG B) Through Day 210[20]

End point description:

The BILAG-2004 index is an organ-specific 97-question assessment based on the principle of the doctor's intent to treat. Only clinical features attributable to SLE disease activity were recorded and based on the subject's condition in the last 4 weeks compared with the previous 4 weeks. It was scored as not present (0), improved (1), the same (2), worse (3), or new (4). Disease activity was graded separately for 9 body systems to 5 different grades (A to E) as follows: A is very active disease, B is moderate activity, C is mild stable disease, D is inactive now but previously active, and E indicates the organ was never involved. A shift from BILAG-2004 Grade A or B to a lower grade indicates a clinically relevant change in disease activity as the BILAG-2004 grades mirror the decision points for treatment interventions. n signifies only the subjects with available data for each time point.

End point type	Secondary

End point timeframe:

Days 30, 60, 90, 120, 150, 180, 210

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Subjects				
number (not applicable)				
Overall (n=37, 75)	6	7		
Day 30 (n = 36, 73)	1	2		
Day 60 (n= 33, 66)	0	0		
Day 90 (n= 33, 65)	2	0		
Day 120 (n = 31, 65)	1	0		
Day 150 (n = 32, 71)	0	1		
Day 180 (n= 34, 71)	1	3		
Day 210 (n = 31, 72)	0	1		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Statistical Analysis 1 for Overall

Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3498
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	-6.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.9
upper limit	9.8

Secondary: Phase 2: Number of Subjects With Physician’s Global Assessment (PGA) Worsening

End point title	Phase 2: Number of Subjects With Physician’s Global Assessment (PGA) Worsening[21]

End point description:

The PGA is used to assess Investigator's general impression on the patient's overall status of SLE disease activity via visual analogue scale (100 mm) with 0 being "very good, asymptomatic and no limitation of normal activities" with 100 mm being "most severe possible disease ever seen in all SLE patients". PGA worsening is defined as an increase of ≥ 30 mm from baseline.

End point type	Secondary

End point timeframe:

Days 30, 60, 90, 120, 150, 180, and 210

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Subjects				
number (not applicable)				
Overall	13	10		
Day 210	10	7		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Statistical analysis for Overall

Comparison groups	Phase 2: Placebo v Phase 2: BOS161721 120 mg

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0072
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	-21.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-36.2
upper limit	-7.4

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Statistical Analysis for Day 210	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0141
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	-17.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-30.9
upper limit	-4.5

Secondary: Phase 2: Number of Subjects With a BILAG-based Composite Lupus Assessment (BICLA) Response at Day 210

End point title	Phase 2: Number of Subjects With a BILAG-based Composite Lupus Assessment (BICLA) Response at Day 210[22]

End point description:

The BICLA is a responder index developed to measure response to therapy, and it includes scores from the BILAG, SLEDAI-2K, and Physician's Global Assessment (PGA). BICLA response is defined as: 1) at least 1 gradation of improvement in baseline BILAG 2004 scores in all body systems with moderate disease activity at entry (eg, all B [moderate disease] scores falling to C [mild], or D [no activity]); 2) no new BILAG A or more than 1 new BILAG B scores; 3) no worsening of total SLEDAI-2K score from baseline; 4) ≤ 10% deterioration in PGA score; and 5) no treatment failure. The PGA is measured on a 0 to 100 mm scale with score 0 to be No Disease Activity and score 100 to be the most Severe Disease Activity.

End point type	Secondary

End point timeframe:

Day 210

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Subjects				
number (not applicable)	12	28		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6107
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	4.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-10.7
upper limit	20.5

Secondary: Phase 2: Number of Subjects With a Cutaneous Lupus Erythematosus Area and Severity Index (CLASI) Response at Day 210

End point title	Phase 2: Number of Subjects With a Cutaneous Lupus Erythematosus Area and Severity Index (CLASI) Response at Day 210[23]

End point description:

The CLASI is a comprehensive tool for assessment of disease activity (CLASI-A) in cutaneous lupus, shown to be valid, reliable, and sensitive to changes in disease activity. Response is defined as at least 50% improvement from baseline in "A" scores. This assessment was applied to all subjects as all were required to have cutaneous disease activity. The total score represents the sum of the individual scores and ranges from 0 to 70. Higher scores are awarded for more severe manifestations.

End point type	Secondary

End point timeframe:

Day 210

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Subjects				
number (not applicable)	16	44		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1237
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	15.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.9
upper limit	31.8

Secondary: Phase 2: Number of Subjects With Medication Failures

End point title	Phase 2: Number of Subjects With Medication Failures[24]

End point description:

Effect of BOS161721 compared with placebo for response on clinical indicators of SLE activity was assessed in adult subjects with moderate to severe SLE on limited background standard of care treatment.
n signifies the number of subjects evaluable at any time (overall assessment) or at the given timepoint (by visit assessment).

End point type	Secondary

End point timeframe:

Days 30, 60, 90, 120, 150, 180, and 210

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Subjects				
number (not applicable)				
Overall (n=37, 75)	9	8		

Day 210 (n= 33, 72)	7	5		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Statistical Analysis for Overall	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0581
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	-13.7
Confidence interval	
level	90 %
sides	2-sided
lower limit	-26.7
upper limit	-0.7

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Statistical Analysis for Day 210	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0471
Method	Pearson’s chi-square test
Parameter estimate	Observed Difference vs. Placebo
Point estimate	-14.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-31.2
upper limit	3.2

Secondary: Phase 2: Mean Change From Baseline in CLASI at Day 210

End point title	Phase 2: Mean Change From Baseline in CLASI at Day 210[25]

End point description:

The CLASI is a comprehensive tool for the assessment of disease activity (CLASI-A) and damage

(CLASI-B) in cutaneous lupus, shown to be valid, reliable, and sensitive to changes in disease activity. Response is defined as 50% improvement from baseline in "A" or "B" scores. This assessment was applied to all subjects as all were required to have cutaneous disease activity. The total score represents the sum of the individual scores and ranges from 0 to 70 (CLASI-A) and 0 to 58 (CLASI-B). Higher scores are awarded for more severe manifestations. Change from baseline was calculated as the post-baseline value minus the baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 210

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Score on a scale				
arithmetic mean (standard deviation)				
CLASI-A (Total Activity)	-4.8 (± 4.08)	-5.2 (± 4.62)		
CLASI-B (Total Damage)	-0.6 (± 2.61)	-0.2 (± 0.90)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Statistical Analysis for CLASI-A (Total Activity)

Comparison groups	Phase 2: Placebo v Phase 2: BOS161721 120 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[26]
P-value	= 0.6596
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	-0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-1.63
upper limit	0.94
Variability estimate	Standard error of the mean
Dispersion value	0.78

Notes:

[26] - This is based on LS Means

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Statistical Analysis for CLASI-B (Total Damage)

Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[27]
P-value	= 0.4105
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	0.3
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.27
upper limit	0.81
Variability estimate	Standard error of the mean
Dispersion value	0.33

Notes:

[27] - This is based on LS Means

Secondary: Phase 2: Mean Change From Baseline in PGA

End point title	Phase 2: Mean Change From Baseline in PGA[28]

End point description:

The PGA is used to assess Investigator's general impression on the patient's overall status of SLE disease activity via visual analogue scale (100 mm) with 0 being "very good, asymptomatic and no limitation of normal activities" with 100 mm being "most severe possible disease ever seen in all SLE patients".

End point type	Secondary

End point timeframe:

Baseline, Day 210

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Score on a scale				
arithmetic mean (standard deviation)	-29.2 (± 20.69)	-28.7 (± 20.35)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Statistical Analysis for Day 210

Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[29]
P-value	= 0.8546
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-6.07
upper limit	7.58
Variability estimate	Standard error of the mean
Dispersion value	4.11

Notes:

[29] - This is based on LS Means

Secondary: Phase 2: Mean Change From Baseline in the Total Number of Swollen Joints, Tender Joints, and Active Joints (Swelling and Tenderness in the Same Joint) in the American College of Rheumatology-28 (ACR-28) Joint Count

End point title	Phase 2: Mean Change From Baseline in the Total Number of Swollen Joints, Tender Joints, and Active Joints (Swelling and Tenderness in the Same Joint) in the American College of Rheumatology-28 (ACR-28) Joint Count[30]

End point description:

The ACR-28 joint count evaluated the number of tender and swollen joints in the shoulder, elbow, wrist, hand, and knee joints. Joints of the feet were excluded. Change from baseline was calculated as the post-baseline value minus the baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 210

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Number of swollen/tender/active joints				
arithmetic mean (standard deviation)				
Sum of Swelling	-6.8 (± 5.17)	-5.9 (± 5.05)		
Sum of Tenderness	-8.3 (± 7.00)	-7.2 (± 5.57)		
Sum of Active Joints	-6.5 (± 5.54)	-5.6 (± 4.65)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Statistical Analysis for Sum of Swelling for Day 210	
Comparison groups	Phase 2: Placebo v Phase 2: BOS161721 120 mg
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[31]
P-value	= 0.4455
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	0.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.63
upper limit	1.71
Variability estimate	Standard error of the mean
Dispersion value	0.7

Notes:

[31] - This is based on LS Means

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
Statistical Analysis for Sum of Tenderness for Day 210	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[32]
P-value	= 0.3367
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	0.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.65
upper limit	2.47
Variability estimate	Standard error of the mean
Dispersion value	0.94

Notes:

[32] - This is based on LS Means

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Statistical Analysis for Sum of Active Joints for Day 210	
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[33]
P-value	= 0.255
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.34
upper limit	1.86
Variability estimate	Standard error of the mean
Dispersion value	0.66

Notes:

[33] - This is based on LS Means

Secondary: Phase 2: Mean Change From Baseline in SLEDAI-2K at Day 210

End point title	Phase 2: Mean Change From Baseline in SLEDAI-2K at Day

End point description:

The SLEDAI-2K is a validated instrument that measures disease activity in SLE subjects at the time of the visit and in the previous 30 days. It is a global index and includes 24 clinical and laboratory variables that are weighted by the type of manifestation, but not by severity. The total score falls between 0 and 105, with higher scores representing increased disease activity. A SLEDAI -2K of 6 or more generally represents moderately to severely active disease. Change from baseline was calculated as the post-baseline value minus the baseline value.

End point type	Secondary

End point timeframe:

Baseline, Day 210

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Score on a scale				
arithmetic mean (standard deviation)	-4.7 (± 3.71)	-3.9 (± 3.31)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[35]
P-value	= 0.2498
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	0.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.34
upper limit	1.93
Variability estimate	Standard error of the mean
Dispersion value	0.68

Notes:

[35] - This is based on LS Means

Secondary: Phase 2: Mean Change From Baseline in Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index

End point title	Phase 2: Mean Change From Baseline in Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index[36]

End point description:

The SLICC/ACR damage index is a validated instrument to assess damage, defined as irreversible impairment, continuously persistent for 6 months (ascertained by clinical assessment), occurring since the onset of lupus, and it is based on a weighted scoring system. This index records damage occurring in subjects with SLE regardless of cause, with demonstrated content, face, criterion, and discriminant validity. A score of 0=no damage. Total maximum score is 47 and increasing score indicates increasing disease severity.
Here, subjects analysed signifies only the subjects with available data for the end point.

End point type	Secondary

End point timeframe:

Baseline; Day 180

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	67		
Units: Score on a scale				
arithmetic mean (standard deviation)	0 (± 0)	0.1 (± 0.24)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Statistical Analysis for Day 180

Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	97
Analysis specification	Pre-specified
Analysis type	superiority[37]
P-value	= 0.2558
Method	ANCOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	0
Confidence interval	
level	90 %
sides	2-sided
lower limit	-0.02
upper limit	0.12
Variability estimate	Standard error of the mean
Dispersion value	0.04

Notes:

[37] - This is based on LS Means

Secondary: Phase 2: Time to Medication Failure

End point title	Phase 2: Time to Medication Failure[38]

End point description:

Subjects who received prohibited medications or undergo unallowable corticosteroid (CS) usage were considered "medication failures".
999.999 = Median was not established based on the number of medication failures observed.

End point type	Secondary

End point timeframe:

Up to Day 270

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Days				
median (confidence interval 90%)	999.999 (999.999 to 999.999)	999.999 (999.999 to 999.999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo

Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[39]
P-value	= 0.0479
Method	Log Rank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.39
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.18
upper limit	0.88

Notes:

[39] - Hazard rate of BOS161721 120 mg / Hazard rate of placebo

Secondary: Mean Percent Change in CS Administration From the Baseline Day 0 Dose Through Day 210 in Subjects Receiving ≥ 7.5 mg/Day Prednisone Equivalent at Day 0

End point title	Mean Percent Change in CS Administration From the Baseline Day 0 Dose Through Day 210 in Subjects Receiving ≥ 7.5 mg/Day Prednisone Equivalent at Day 0[40]

End point description:

The percent reduction in CS administration from Day 0 through Day 210 was determined based on the average daily CS usage.
Here, subjects analysed signifies only the subjects with available data for the end point.

End point type	Secondary

End point timeframe:

Baseline; Day 210

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	13	45		
Units: Percent Reduction in Dose (mg/day)				
arithmetic mean (standard deviation)	-36.61 (± 22.389)	-21.49 (± 26.950)		

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Longest SRI-4 Response

End point title	Phase 2: Duration of Longest SRI-4 Response[41]

End point description:

The SRI-4 is a composite index of SLE disease improvement that consists of scores derived from

SLEDAI-2K, BILAG 2004 Index and PGA. Response based on the SRI-4 is defined by: 1) ≥ 4-point reduction in the SLEDAI-2K total score; 2) no new severe disease activity (BILAG A organ score) or more than 1 new moderate organ score (BILAG B) compare with baseline; and 3) no deterioration from baseline in the PGA by ≥ 30 millimeters. The total SLEDAI-2K score falls between 0 and 105, with higher scores representing increased disease activity. The PGA is used to assess Investigator's general impression on the patient's overall status of SLE disease activity via visual analogue scale (100 mm) with 0 being "very good, asymptomatic and no limitation of normal activities" with 100 mm being "most severe possible disease ever seen in all SLE patients". The SRI-4 response in subjects with moderate to severe SLE is associated with broad improvements in clinical and subject-reported outcomes.

End point type	Secondary

End point timeframe:

Up to Day 270

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Days				
arithmetic mean (standard deviation)	119.8 (± 68.26)	124.2 (± 68.48)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[42]
P-value	= 0.7898
Method	ANOVA
Parameter estimate	Treatment Difference (BOS161721-Placebo)
Point estimate	4.4
Confidence interval	
level	90 %
sides	2-sided
lower limit	-22.92
upper limit	31.7
Variability estimate	Standard error of the mean
Dispersion value	16.4

Notes:

[42] - This is based on LS Means

Secondary: Phase 2: Time to First BILAG Flare (≥ 1 New or Recurrent BILAG A or > 1 New or Recurrent BILAG B) Relative to Baseline Through Day 210

End point title	Phase 2: Time to First BILAG Flare (≥ 1 New or Recurrent BILAG A or > 1 New or Recurrent BILAG B) Relative to Baseline Through Day 210[43]

End point description:

The BILAG-2004 index is an organ-specific 97-question assessment based on the principle of the doctor's intent to treat. Only clinical features attributable to SLE disease activity were recorded and based on the subject's condition in the last 4 weeks compared with the previous 4 weeks. It was scored as not present (0), improved (1), the same (2), worse (3), or new (4). Disease activity was graded separately for 9 body systems to 5 different grades (A to E) as follows: A is very active disease, B is moderate activity, C is mild stable disease, D is inactive now but previously active, and E indicates the organ was never involved. A shift from BILAG-2004 Grade A or B to a lower grade indicates a clinically relevant change in disease activity as the BILAG-2004 grades mirror the decision points for treatment interventions.
999.999 = Median was not established based on the number of BILAG flares observed.

End point type	Secondary

End point timeframe:

Baseline; Day 210

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	75		
Units: Days				
median (confidence interval 90%)	999.999 (999.999 to 999.999)	999.999 (999.999 to 999.999)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Phase 2: BOS161721 120 mg v Phase 2: Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority[44]
P-value	= 0.0083
Method	Log-Rank Test (2-Sided)
Parameter estimate	Hazard ratio (HR)
Point estimate	0.33
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.16
upper limit	0.68

Notes:

[44] - Hazard rate of BOS161721 120mg / Hazard rate of placebo

Secondary: Phase 2: Number of Subjects With AEs

End point title	Phase 2: Number of Subjects With AEs[45]

End point description:

The safety and tolerability of repeat doses of BOS161721 (120 mg) administered SC were assessed in

adult subjects with moderate to severe SLE on limited background standard of care treatment.

End point type	Secondary

End point timeframe:

Up to Day 270

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint is the secondary endpoint for Phase 2 only

End point values	Phase 2: Placebo	Phase 2: BOS161721 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	76		
Units: Subjects				
number (not applicable)				
Any TEAE	23	44		
Related TEAE	4	8		
Serious TEAE	3	2		
Related Serious TEAE	0	0		
Any CTCAE Grade 2 or Higher TEAE	16	25		
Any Related CTCAE Grade 2 or Higher TEAE	0	3		
Any CTCAE Grade 3 TEAE	3	6		
Any Related CTCAE Grade 3 or Higher TEAE	0	0		
Any CTCAE Grade 4 TEAE	0	0		
Any Related CTCAE Grade 4 TEAE	0	0		
TEAE Leading to Discontinuation of Study Treatment	1	0		
Related TEAE Leading to Discont of Study Treatment	0	0		
TEAE of Special Interest	0	1		
Related TEAE of Special Interest	0	0		
Dose-Limiting Toxicity	0	0		
Related Dose-Limiting Toxicity	0	0		
TEAE Resulting in Death	0	0		
Related TEAE Resulting in Death	0	0		
Injection Site Reaction	1	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to Day 270

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Phase 1b: Placebo

Reporting group description:

Subjects were randomized to receive subcutaneous (SC) dose of placebo. Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits at Days 210, 240, and 270.

Reporting group title	Phase 1b: Cohort 1: BOS161721 20 mg

Reporting group description:

Subjects were randomized to receive a 20 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Reporting group title	Phase 1b: Cohort 2: BOS161721 60 mg

Reporting group description:

subjects were randomized to receive a 60 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270

Reporting group title	Phase 1b: Cohort 3: BOS161721 120 mg

Reporting group description:

Subjects were randomized to receive a 120 mg SC dose of BOS161721. Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Reporting group title	Phase 2: Placebo

Reporting group description:

Subjects were randomized to receive a SC dose of placebo (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of placebo on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Reporting group title	Phase 2: BOS161721 120 mg

Reporting group description:

Subjects were randomized to receive a 120 mg SC dose of BOS161721 (as determined from Phase 1b of the study). Subjects received a total of 7 SC monthly doses of BOS161721 on Days 0, 30, 60, 90, 120, 150, and 180, followed by safety follow-up visits on at Days 210, 240, and 270.

Serious adverse events	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	2 / 9 (22.22%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Exomphalos			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			

subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus pneumonitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis acute			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1b: Cohort 3: BOS161721 120 mg	Phase 2: Placebo	Phase 2: BOS161721 120 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 9 (0.00%)	3 / 37 (8.11%)	2 / 76 (2.63%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraductal proliferative breast lesion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			

subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Exomphalos			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lupus pneumonitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary colic			

subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Phase 1b: Placebo	Phase 1b: Cohort 1: BOS161721 20 mg	Phase 1b: Cohort 2: BOS161721 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 7 (57.14%)	2 / 5 (40.00%)	7 / 9 (77.78%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	1 / 9 (11.11%)
occurrences (all)	0	1	1
Deep vein thrombosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Adnexa uteri pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Cough			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Pulmonary hypertension			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Investigations			
White blood cells urine positive			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	2
Blood pressure increased			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Animal bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Ankle fracture			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Migraine			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Cervical radiculopathy			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Diplopia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Nausea			

subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	2	0	1
Diarrhoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Dental caries			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	1	0	1
Bursitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Fibromyalgia			

subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Sjogren's syndrome			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	3	0
Pharyngitis			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Cervicitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Diverticulitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	1	0	0
Herpes zoster			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Infected bite			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Nasal abscess			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	1 / 9 (11.11%)
occurrences (all)	0	0	1
Otitis media acute			
subjects affected / exposed	0 / 7 (0.00%)	1 / 5 (20.00%)	0 / 9 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 5 (0.00%)	0 / 9 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1b: Cohort 3: BOS161721 120 mg	Phase 2: Placebo	Phase 2: BOS161721 120 mg

Total subjects affected by non-serious adverse events subjects affected / exposed	8 / 9 (88.89%)	22 / 37 (59.46%)	44 / 76 (57.89%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	2 / 76 (2.63%)
occurrences (all)	0	1	4
Deep vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	2 / 9 (22.22%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences (all)	2	1	0
Reproductive system and breast disorders			
Menorrhagia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 37 (5.41%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Adnexa uteri pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	2	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Depression			

subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Investigations			
White blood cells urine positive			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	2 / 76 (2.63%)
occurrences (all)	0	2	5
Blood pressure increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Weight increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Animal bite			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Ankle fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Bundle branch block right			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 9 (0.00%)	2 / 37 (5.41%)	4 / 76 (5.26%)
occurrences (all)	0	2	6

Migraine			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	1 / 76 (1.32%)
occurrences (all)	0	1	1
Cervical radiculopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 37 (5.41%)	0 / 76 (0.00%)
occurrences (all)	0	2	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 9 (22.22%)	1 / 37 (2.70%)	4 / 76 (5.26%)
occurrences (all)	2	2	4
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	3 / 37 (8.11%)	1 / 76 (1.32%)
occurrences (all)	0	3	1
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	2 / 76 (2.63%)
occurrences (all)	0	1	2
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Abdominal pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Dental caries			

subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Tongue ulceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 9 (0.00%)	3 / 37 (8.11%)	2 / 76 (2.63%)
occurrences (all)	0	4	2
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Bursitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	3 / 76 (3.95%)
occurrences (all)	1	0	3
Fibromyalgia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Muscle spasms			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	2	0	0
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Sjogren's syndrome			
subjects affected / exposed	0 / 9 (0.00%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	3 / 37 (8.11%)	7 / 76 (9.21%)
occurrences (all)	0	4	9
Urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	4 / 37 (10.81%)	4 / 76 (5.26%)
occurrences (all)	0	4	6
Pharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 37 (5.41%)	4 / 76 (5.26%)
occurrences (all)	0	2	4
Upper respiratory tract infection			
subjects affected / exposed	2 / 9 (22.22%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences (all)	2	1	0
Bronchitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	2 / 76 (2.63%)
occurrences (all)	1	0	2
Escherichia urinary tract infection			
subjects affected / exposed	0 / 9 (0.00%)	2 / 37 (5.41%)	1 / 76 (1.32%)
occurrences (all)	0	2	1
Cervicitis			
subjects affected / exposed	1 / 9 (11.11%)	1 / 37 (2.70%)	0 / 76 (0.00%)
occurrences (all)	1	1	0
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1
Vulvovaginal mycotic infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	0	0	1
Diverticulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0

Infected bite			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Nasal abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Otitis media acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	3	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	0 / 76 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 9 (11.11%)	0 / 37 (0.00%)	1 / 76 (1.32%)
occurrences (all)	1	0	1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 November 2017	Protocol Amendment 1: For clarity, site visits are based on study day number only; Clarification and updated with new safety data; Clarification to correct level of exposure; Removed erroneous text and added clarity that Boston Pharmaceuticals will review data along with DMC for POC Dose selection; Clarification to allow flexibility in exact number enrolled; Dose modifications/ adjustments are not allowed in this study; Screening for POC study can begin while dose decision is being made; Text removed as Boston Pharmaceuticals will be reviewing biomarker data for POC dose selection; Clarification (genotype needed to establish gene signature); text added to clarify how the subject should complete the study; text removed as efficacy data were to be reviewed by Boston Pharmaceuticals in order to make informed dose selection decision.
21 March 2018	Protocol Amendment 2: Replaced 'subjects' to 'patients' since the enrolled participants are with SLE condition; Clarification that POC dose selection will be based on DMC and sponsor assessment; Updated for clarity and to provide a comprehensive list of endpoints identified in the protocol; Clarification on POC sample size; Text updated to clarify that a minimum BILAG 1 'A' or 2 'B' scores is required for screening; Text was added to clarify randomization and blinding process; Clarified that no need for predose injection site reaction assessment at baseline; Text updated to clarify new number of dropouts assumed for the study; Clarify that Grades 2 to 5 injection site reactions are AEs of special interest; Updated to clarify the planned PD assessments; updates done to statistical sections.
27 July 2018	Protocol Amendment 3: Text added to clarify that MAD and POC are 2 portions of this 1 study and not 2 separate studies; updates done for Protocol clarification; updates done for statistical clarification; updates done to include more data from the 120 mg cohort in data review to determine POC dose; updates done to inclusion/exclusion criteria; Urine pregnancy test added at day 270 to ensure patient is not pregnant at end of 90 day follow-up due to 41 day half-life of study drug; Added end of study definitions; Added text to ensure eligibility prior to randomization; Added definition of worsening PGA.
23 January 2019	Protocol Amendment 4: Changes done to correct the error in the previous version; updates done for protocol clarification; Added text for POC dose and justification; Text added 1) to clarify that basal cell carcinoma is not a neoplasia associated with immune suppression, but rather secondary to sun exposure and 2) to clarify specific opportunistic infections of special interest in this study.
23 July 2019	Protocol Amendment 5: Updates done for protocol clarification, Changes done to Objectives and Endpoints; Changes done to Criteria for Inclusion and Exclusion to ensure subjects with moderate to severe active disease are enrolled; provided further clarification that the central eligibility review team can deem a subject in-eligible for randomization even if all entrance criteria are met; Added for opioid dosing in SLE subjects.
30 April 2020	Protocol Amendment 6: This amendment summarizes the measures implemented during the COVID-19 pandemic to protect patient safety and data integrity: Safety oversight: In case a subject cannot return to the study site for the scheduled visit, the site staff will contact the subject remotely for safety follow-up; Central Laboratory: In the case that there are courier issues that will prevent the protocol-required laboratory specimens to be sent to the study core laboratory, the site should have the safety laboratory specimens; Investigational Product Dosing: In cases when dosing cannot be performed during the protocol-designated windows, the Investigator should discuss each case with the Sponsor to determine whether it is a missed visit or whether the dosing can be performed outside protocol windows.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported